



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/US91/01714 (22) International Filing Date: 14 March 1991 (14.03.91) (30) Priority data: 493,309 14 March 1990 (14.03.90) US (60) Parent Application or Grant (63) Related by Continuation US 493,309 (CIP) Filed on 14 March 1990 (14.03.90) (71) Applicant (for all designated States except US): CANDELA LASER CORPORATION [US/US]; 530 Boston Post Road, Wayland, MA 01778 (US).</p>		<p>(72) Inventors; and (75) Inventors/Applicants (for US only) : FURUMOTO, Horace [US/US]; 14 Woodridge Road, Wellesley, MA 02181 (US). CECCON, Harry, L. [US/US]; 8 Bond Street, Boston, MA 02118 (US). JONES, Christopher, J. [US/ US]; 18 Brookside Avenue, Lexington, MA 02173 (US). McMILLAN, Kathleen [US/US]; 16 Royal Crest Drive, #8, Marlboro, MA 01752 (US).  (74) Agents: SMITH, James, M. et al.; Hamilton, Brook, Smith &amp; Reynolds, Two Militia Drive, Lexington, MA 02173 (US).  (81) Designated States: AT (European patent), AU, BE (Euro- pean patent), BR, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (Eu- ropean patent), IT (European patent), JP, LU (European patent), NL (European patent), SE (European patent), US.  Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>
<p>(54) Title: APPARATUS FOR TREATING ABNORMAL PIGMENTATION OF THE SKIN</p> <div data-bbox="646 1201 1079 1596" data-label="Image"> </div> <p>(57) Abstract</p> <p>An apparatus comprises a first pulsed laser producing a beam of laser radiation having a wavelength between 345 and 600 nm for the treatment of epidermal pigmented lesions and a second pulsed laser producing a beam of laser radiation having a wavelength between 600 and 1100 nm for the treatment of dermal pigmented lesions. A delivery system is coupled to the apparatus and manipulated to deliver radiation to illuminate an area of a subject's skin. The delivery system of the present invention comprises a pair of flexible liquid core light guides having sufficient diameter to efficiently transmit high peak power intensity pulses of wavelengths between 345 and 1100 nm. For treatment of epidermal pigmented lesions, a first liquid core light guide delivers laser radiation of between 345 and 600 nm and preferably about 500 nm wavelength. The fluence is between 1 and 10 J/cm<sup>2</sup> at the skin and preferably between 2 and 4 J/cm<sup>2</sup>. The pulse duration is less than 1 μsec and preferably less than 500 nsec. A 2 to 5 mm diameter spot is illuminated. For treatment of dermal pigmented lesions such as tattoos, a second liquid core light guide delivers laser radiation of between 600 and 1100 nm, fluence is between 1 and 10 J/cm<sup>2</sup> at the skin, pulse duration is less than 500. Once again, a 2 to 5 mm diameter spot is illuminated.</p>		



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<p><b>(54) Title:</b> APPARATUS FOR TREATING ABNORMAL PIGMENTATION OF THE SKIN</p> <div style="text-align: center; margin: 20px 0;"> </div> <p><b>(57) Abstract</b></p> <p>An apparatus comprises a first pulsed laser producing a beam of laser radiation having a wavelength between 345 and 600 nm for the treatment of epidermal pigmented lesions and a second pulsed laser producing a beam of laser radiation having a wavelength between 600 and 1100 nm for the treatment of dermal pigmented lesions. A delivery system is coupled to the apparatus and manipulated to deliver radiation to illuminate an area of a subject's skin. The delivery system of the present invention comprises a pair of flexible liquid core light guides having sufficient diameter to efficiently transmit high peak power intensity pulses of wavelengths between 345 and 1100 nm. For treatment of epidermal pigmented lesions, a first liquid core light guide delivers laser radiation of between 345 and 600 nm and preferably about 500 nm wavelength. The fluence is between 1 and 10 J/cm<sup>2</sup> at the skin and preferably between 2 and 4 J/cm<sup>2</sup>. The pulse duration is less than 1 µsec and preferably less than 500 nsec. A 2 to 5 mm diameter spot is illuminated. For treatment of dermal pigmented lesions such as tattoos, a second liquid core light guide delivers laser radiation of between 600 and 1100 nm, fluence is between 1 and 10 J/cm<sup>2</sup> at the skin, pulse duration is less than 500. Once again, a 2 to 5 mm diameter spot is illuminated.</p>				

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APPARATUS FOR TREATING ABNORMAL  
PIGMENTATION OF THE SKIN

Background of the Invention

Abnormal pigmentation of the skin is commonly seen  
5 in dermatologic practice. A subject's skin may have  
pigmentation abnormalities due to vascular lesions,  
naturally occurring pigmented lesions, or tattoos.  
Vascular lesions such as port wine stain birthmarks,  
telangiectasia and hemangiomas are caused by the  
10 abundance of enlarged blood vessels. Pigmented lesions  
are non-vascular disfigurements of the skin caused by an  
abnormally high concentration of melanin in localized  
areas of the skin. Such pigmented lesions include  
freckles, age or liver spots, cafe' au lait birthmarks,  
15 lentigines, nevi, melanomes, nevus of Ota and lentigo  
maligna. Tattoos may be divided into two categories,  
including self-inflicted or traumatic tattoos. Traumatic  
tattoos are created during accidents which cause a scrape  
or abrasion such that a foreign material becomes imbedded  
20 in the skin.

A myriad of therapeutic modalities including liquid  
nitrogen, electrocautery and depigmenting chemicals have  
been used to remove superficial pigmented lesions.  
Although widely used, none have succeeded in destroying  
25 the abnormal pigmented cells alone without damaging  
adjacent structures and producing adverse effects like  
hypopigmentation.

Over the last two decades, there have been several  
reports describing the removal of superficial pigmented  
30 lesions by a variety of lasers such as the excimer (351

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nm), argon (488,514 nm), ruby (694 nm), Nd:YAG (1060 nm), and CO<sub>2</sub> (10,600 nm) lasers. However, there has generally been damage to both pigmented and nonpigmented cells. Pigmented lesions treated by laser have included

5 lentigines, nevi, melanomas, oral hypermelanosis of Peutz-Jeghers syndrome, the nevus of Ota, and a lentigo maligna. The pigment depth of these laser-treated lesions has also varied significantly, from superficial lentigines in the epidermis to lesions lying deep in the

10 reticular dermis like the nevus of Ota.

Previous studies reporting "successful" removal of pigmented lesions have relied on clinical assessment rather than on histology and have used widely divergent wavelengths, pulse durations, energy densities and

15 spotsizes. There has been no effort to define laser parameters necessary for optimal removal of pigmented lesions.

Melanin, an endogenous cutaneous pigment which is most concentrated in the basal layer of the epidermis,

20 has an absorption spectrum that is highest in the ultraviolet range and gradually diminishes toward the infrared. Melanosomes are melanocyte-specific organelles densely packed with melanin. They vary in size according to their genetic origin; black skin typically containing

25 larger melanosomes than lightly pigmented, white skin. Based on melanosome size, the calculated thermal relaxation time for these organelles is around 10 nsec. On the other hand, melanocytes are approximately 7  $\mu$ m in diameter, with thermal relaxation times around 1  $\mu$ sec.

30 Thermal relaxation time in both instances is defined as the time taken for a structure to cool to 50% of its peak temperature immediately after laser exposure.

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Recent studies have applied the technique of selective photothermolysis to specifically destroy melanosomes using the XeF pulsed excimer in vitro and the Q-switched ruby lasers in vivo. Histologically, both  
5 these studies demonstrated melanosomal injury that was associated with disruption of melanocytes as well as melanin-containing basal keratinocytes. In addition, there was also evidence of follicular damage after exposure of pigmented guinea pig skin to the Q-switched  
10 ruby laser.

Selective photothermolysis has also been employed in other studies to treat tattoos. It was demonstrated that a Q-switched ruby laser is not effective for all types of tattoos, because tattoos are often multicolored. These  
15 studies have shown that blue-black tattoos responded well to Q-switched ruby laser treatment, while green and yellow tattoos responded less than well and red tattoos responded poorly or not at all. Additionally, persistent hypopigmentation was a frequent occurrence.

#### 20 Disclosure of the Invention

In accordance with the present invention, an apparatus produces a plurality of pulsed beams of laser radiation for the treatment of epidermal and dermal pigmentation abnormalities of the skin. By having the  
25 capability to provide plural laser beams of different wavelengths (colors), the range of applications for which the apparatus is effective increases significantly. An apparatus capable of providing one of two beams of different wavelengths is believed to be sufficiently  
30 effective for the majority of cases in therapeutic dermatology and plastic surgery involving treatment of non-vascular pigmentation abnormalities.

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The apparatus comprises a first pulsed laser producing a first beam principally for the treatment of epidermal pigmentation abnormalities and a second pulsed laser producing a second beam principally for the treatment of dermal pigmentation abnormalities. In one embodiment, the first laser is pulsed dye laser supported by a dye circulation system and the second laser is an alexandrite laser. The two lasers are coupled to a common power supply and storage system. The lasers are excited by a flashlamp means which may comprise a single coaxial flashlamp for exciting both lasers or a pair of coaxial flashlamps for separately exciting each laser. In another embodiment, the first laser is used to excite the second laser in a laser excited configuration. In this embodiment, the first laser is preferably a flashlamp excited pulsed dye laser and the second laser is preferably an alexandrite laser.

In accordance with one feature of the present invention, specific laser parameters are established to obtain effective treatment of epidermal and dermal pigmentation abnormalities while minimizing damage to normal pigmented cells. To that end, effective treatment of epidermal lesions with minimal damage has been obtained with a first laser having a wavelength of about 500 nm, a pulse duration of about 500 nsec, and fluence (energy density) of about  $3 \text{ J/cm}^2$  at the skin. The spotsize may range from about 2 to 5 mm diameter, but preferably it is about 3 mm diameter. To minimize damage, wavelength of the first beam should be less than 600 nm. Due to known problems of mutagenesis, the wavelength should not be less than 345 nm. The fluence of the first beam may range from 1 to  $10 \text{ J/cm}^2$  at the skin through the full range of wavelengths, but is

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preferably within the range of 2 to 4 J/cm<sup>2</sup> for 504 nm light. Pulse durations approaching 1 μsec may be used but at 1 μsec recurrence is expected. Shorter pulse durations should minimize damage to normal tissue.

5 To avoid pigmentary incontinence of the epidermal pigment resulting from laser irradiation and to get better access to dermal pigment to effectively treat dermal pigmentation abnormalities, a window is created in the epidermis using the above defined laser parameters  
10 and the deeper cells are treated with the second laser having parameters specific to those cells. More specifically, it is expected that effective treatment with minimal damage may be obtained with the second laser having a wavelength of about 750 nm, a pulse duration of  
15 about 100 nsec and an energy of about 1 J/cm<sup>2</sup> at the skin. The fluence at the skin for the second beam may range from 1 to 10 J/cm<sup>2</sup> through a range of wavelengths between 600 and 1100 nm, but it is preferably within the range of 1 to 4 J/cm<sup>2</sup> for 760 nm light. The spotsize may  
20 range from about 2 to 5 mm diameter, but preferably it is about 3 mm diameter. The longer wavelengths are required to penetrate to depths associated with the location of dermal pigmentation abnormalities.

In a typical dermatology procedure, treatment is  
25 administered with a delivery system which is manipulated to deliver radiation to illuminate an area of a subject's skin. For effective treatment, the dual laser system requires pulse durations on the order of tens to hundreds of nanoseconds for potentially high intensity pulses.  
30 Thus, the delivery system must be capable of transmitting high peak intensity pulses with low losses and must be flexible for convenience of use.



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To that end, one embodiment of the preferred delivery system of the present invention comprises a pair of flexible liquid core light guides having sufficient diameter to efficiently transmit high peak power intensity pulses of wavelengths between 345 and 1100 nm from the dual laser system. More specifically, a first liquid core light guide delivers the first beam of laser radiation of wavelength between 345 and 600 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 1  $\mu$ sec to the handpiece for treatment of epidermal pigmented lesions. The first liquid core light guide has a liquid core comprising an aqueous inorganic salt solution within a flexible cladding which facilitates the transmission of laser radiation of wavelengths between 345 and 600 nm. The core diameter may be between 3 and 10 mm and preferably about 3 mm such that the first guide is capable of transmitting high peak intensity pulses. However, the liquid within the first guide does not effectively transmit radiation of wavelengths between 600 and 1100 nm due to the presence of chemical bonds involving hydrogen which significantly attenuate the radiation.

The second liquid core light guide delivers the second beam of laser radiation of wavelength between 600 and 1100 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 500 nsec to the handpiece for treatment of dermal pigmentation abnormalities such as tattoos. The second guide has a liquid core comprising a liquid and housed within a flexible cladding. The liquid has a molecular structure characterized by the absence of chemical bonds which would cause absorption between wavelengths 600 and 1100 nm. As a minimum, the liquid is non-hydrogenous and comprises halogenated compounds.

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5        Preferably, the liquid comprises halocarbons such as tetrachloroethylene or carbon tetrachloride, or a solution of inorganic salts in deuterium oxide. The index of refraction for the liquid is greater than the index of refraction for the cladding. The liquid core of the second light guide has a diameter between 3 and 10 mm and preferably about 5 mm such that the second guide is capable of transmitting high peak intensity pulses.

10        Another embodiment of the preferred delivery system of the present invention comprises a flexible liquid core light guide for efficiently transmitting high peak power intensity pulses of wavelengths between 345 and 1100 nm from the dual laser system. More specifically, the second light guide comprises a liquid capable of  
15        delivering laser radiation from the first laser for treatment of epidermal pigmentation abnormalities and from the second laser for treatment of dermal pigmentation abnormalities. In this embodiment, the light guide is coupled to both lasers and delivers  
20        radiation from the particular laser being employed for treatment.

Other advantages and features of the invention will become apparent from the following description of the preferred embodiments, and from the claims.

25        Brief Description of the Drawings

Fig. 1 illustrates a dual laser system with separate delivery systems.

Fig. 2 is an enlarged perspective view of the handpiece of Fig. 1.

30        Fig. 3 is a block diagram of a preferred embodiment dual laser system.

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Fig. 4 is a block diagram of another preferred embodiment dual laser system.

Fig. 5 is a block diagram of yet another preferred embodiment dual laser system.

5 Fig. 6 is a cross-sectional view of a liquid core light guide of Fig. 1.

#### Description of Preferred Embodiments

Pigmentation abnormalities may be removed from the skin by lasers provided that the lasers have the proper characteristics based on the principles of selective photothermolysis. These principles require the proper selection of wavelength (or color) of the laser to maximize absorption within the targeted lesion and minimize absorption by the surrounding normal tissue, organs or organelles. Selective photothermolysis also requires the precise selection of pulse duration of the laser beam which is determined by the thermal relaxation time of the target. Pulse duration should be shorter than the thermal relaxation so that only the targeted material is heated and the surrounding tissue is unaffected.

Pigmented lesions have broad band absorption characteristics with high absorption at shorter wavelengths (blue-violet) and decreasing monotonically to higher wavelengths (red). Additionally, it has been shown that shorter wavelength (blue-green) lasers treat superficial pigmented lesions better than longer wavelength (red) lasers. On the other hand, longer wavelength (red) lasers are more effective for treating dermal pigmentation abnormalities including deeper pigmented lesions and tattoos. However, it has been demonstrated that the long wavelength ruby red laser is

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not effective for tattoos. Blue and black tattoos respond well to ruby laser treatment, while green and yellow tattoos respond less well and red tattoos respond poorly. These results are predicable based on the absorption characteristics of the tattoo pigments. It is therefore desirable to tailor the wavelength (color) of the laser radiation to the absorption characteristic of the targeted material within the skin.

In accordance with the present invention, a laser system 12 provides two pulsed beams of laser radiation having distinct wavelengths which may be employed for the treatment of epidermal and dermal pigmented lesions of the skin (see Fig. 1). Although a laser system producing more than two different wavelength beams is within the scope of this invention, discussion is limited to a laser system providing two different wavelength pulsed beams. Also, the specific parameters of each laser beam including wavelength, intensity and pulse duration are discussed in detail below.

A delivery system 13 is coupled to the laser system 12 and delivers the two laser beams to a pigmented region of the skin. In a preferred embodiment, the first laser beam is delivered through a first light guide 14 to a handpiece 16 and second laser beam is delivered through a second light guide 15 to a handpiece 17. In another preferred embodiment, the delivery system may comprise only the second light guide 15 and the handpiece 17 (Fig. 5). In this embodiment, both laser beams are coupled to the guide 15 which delivers either beam to the skin for treatment of pigmentation abnormalities. Alternatively, one or both laser beams may be delivered through an articulated arm (not shown). The features of the first and second light guides are discussed in detail below. A

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preferred handpiece, illustrated in Fig. 2, is model number 7040-00-6231 sold by Candela Laser Corporation. Two lenses in the handpiece image the distal end of the guide to a larger spot adjacent to the end of a positioning extension 18. By selection of the lenses, the spotsize can be varied. The spotsize may be between 2 and 5 mm diameter and is preferably about 3 mm diameter. By movement of the handpiece and irradiation of adjacent spots, a test site of about 0.5-1.0 cm x 0.5-1.0 cm may be irradiated at a selected dose.

In a preferred embodiment of the laser system, as shown in Fig. 3, the laser system 12 comprises a pair of laser systems 20 and 22. The laser systems comprise a pair of flashlamp excited pulsed lasers 21 and 23 having a common power supply/storage system 24. The lasers are excited by a flashlamp means which may comprise a single coaxial flashlamp (not shown) or a pair of coaxial flashlamps 26 and 27 for separately exciting the first and second laser 21 and 23 respectively. Preferably, the first laser 21 is a pulsed dye laser having a dye circulation system 28 and the second laser 23 is an alexandrite laser. Alternatively, both lasers may be pulsed dye lasers with separate circulation systems. Furthermore, one or both of the laser systems 20 and 22 may comprise any non-dye pulsed laser system such as a solid state laser.

In another preferred embodiment, shown in Fig. 4, a first laser system 20 is arranged to excite a second laser system 22 in a laser-excited configuration. Preferably, the first laser 20 is a flashlamp excited pulsed dye laser supported by a dye circulation system 28 and the second laser 32 is an alexandrite laser. In yet another preferred embodiment, shown in Fig. 5, the pair

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of laser systems 20 and 22 are coupled by an optical coupler 38 to the delivery system 13 comprising a single light guide 17. In any of the preferred embodiments, the laser systems 20 and 22 may comprise any combination of the following lasers to provide a short wavelength beam and a long wavelength beam of laser radiation. Accordingly, the first laser may be a dye laser, or a frequency doubled Neodymium, Nd:YAG, Nd:Glass, Nd:YLF, Ti:Sapphire, frequency doubled Alexandrite or excimer laser. The second laser may be a dye laser or a solid state laser including a ruby, Ti:Sapphire,  $\text{SM}^3$ :YLF or any chromium laser in assorted host materials  $\text{KZnF}_3$ ,  $\text{ScBO}_3$ , LaLuGG, GSGG, YSGG, YGG,  $\text{BeAl}_2(\text{SO}_3)_6$ .

Specific laser parameters have been established for the dual laser system to obtain effective treatment of epidermal and dermal pigmented lesions while minimizing damage to normal pigmented cells and are hereinafter discussed.

A wide range of experimental treatments have been performed on the normally pigmented skin of miniature black pigs and those have been followed by extensive clinical studies. A first set of experiments was performed to identify shorter wavelengths in the green portion of the spectrum for the minimization of epidermal damage, particularly pigmentary incontinence, as well as regeneration of normal pigment cells. A second set of experiments using the optimum laser wavelength of 504 nm has identified shorter pulse durations as preferred for minimizing epidermal damage. Finally, clinical studies of human patients have demonstrated that laser light of the shorter wavelengths and shorter pulse durations is most effective in treating the epidermal pigmented lesions with treatment fluences at the skin of about 3

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J/cm<sup>2</sup>. Limited human pigmented lesion studies have demonstrated lack of effectiveness in treating epidermal pigmented lesions at 694 nm and 750 nm.

In the experiments related to epidermal (superficial) pigmented lesions, a Model SLL500-M flashlamp-pumped tunable dye laser system supplied by Candela Laser Corporation has been used. The light was delivered through a 1 mm diameter optical fiber cable to a handpiece to illuminate a spot of 1 to 3 mm diameter with a single pulse. The handpiece used was a model number 7040-00-6231 supplied by Candela Laser Corporation.

In the first set of experiments on normal black pig skin, the tunable dye laser was tuned to 504, 590, 694, 720 and 750 nm using a variety of dye mixtures. The laser had a pulse duration of 500 nsec. Energy densities ranging from .25 to 3.0 J/cm<sup>2</sup> at 0.25 J/cm<sup>2</sup> increments, and at 4.0, 5.0, 6.0 and 7.0 J/cm<sup>2</sup> were delivered to pigmented skin at a spotsize of 3 mm diameter. The skin was irradiated at each energy density for each of the five wavelengths tested. Skin biopsies were taken at each energy density from each of the five wavelengths immediately and at 4, 16, 23 and 33 days after laser exposure. These experiments were published by Sherwood et al., "Effect of wavelength on cutaneous pigment using pulsed irradiation," The Journal of Investigative Dermatology, Vol. 92, No. 5, May 1989.

Exposure of skin to energy densities of at least 5 J/cm<sup>2</sup> for 590 and 694 nm and 4.0 J/cm<sup>2</sup> for 720 and 750 nm resulted in sub-epidermal clefts accompanied by epidermal necrosis. No sub-epidermal clefts or epidermal necrosis were observed after exposure of skin to 504 nm irradiation, not even at the highest energy density of

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7.0 J/cm<sup>2</sup>. In addition to epidermal injury, dermal damage consisting of collagen bundle separation accompanied by changes in the tinctorial quality of the bundles were observed in biopsies taken from the skin exposed to 7.0 J/cm<sup>2</sup> at the four wavelengths other than 504 nm. The extent of dermal injury appeared dependent on the wavelength; the most severe occurring at 750 nm. From biopsies, pigmentary incontinence (pigment dropping to the dermal layer) was evident. Its severity increased with increased energy density and wavelength.

Although pigment was destroyed using all wavelengths, repigmentation occurred more rapidly for the 504 nm irradiation. For the 504 nm irradiation, repigmentation was complete by the thirty-third day after exposure. Repigmentation followed sequentially by order of wavelength, with the 750 nm irradiated skin taking up to six weeks for its pigment to return to normal.

In the second set of experiments, miniature black pig skin was again irradiated. Using a 504 nm laser and 3 mm diameter spotsize, the effect of pulse durations of 100, 150, 250 and 500 nsec at fluences from 1.5 to 4.0 J/cm<sup>2</sup>, at 0.5 J/cm<sup>2</sup> increments, were examined. Biopsies were taken immediately and at 7, 14 and 28 days after irradiation and were processed for light microscopy. The most severe damage was observed in skin exposed to pulse durations of 250 and 500 nsec. Epidermal necrosis, dermal-epidermal separation and pigmentary incontinence were not only more severe, but also occurred at significantly lower fluences than was evident in skin exposed to 100 and 150 nsec pulse durations. Although the normal cells repigment, the unsightly damage remains.

In the final clinical studies with human patients, superficial benign cutaneous pigmented lesions had been



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5 treated by using the pulse irradiation. Fifty-two patients have been treated variously for the following: lentigines, solar keratoses/'lentignes', cafe' au lait, seborrheic keratoses, hyperpigmentation associated with morphoea, nevus spilus.

Generally, the superficial lesions have been exposed to 504 nm laser irradiation. Pulse durations of 250 nsec, 500 nsec and 1  $\mu$ sec have been used with fluence ranging from 1.5 to 3.5 J/cm<sup>2</sup> for each pulse duration. A 3 mm diameter spotsize was used with the 500 nsec and 1  $\mu$ sec pulse durations. Because of limits in energy available from the particular laser used, a 2 mm diameter spotsize was used with 250 nsec pulse durations. A 1 mm diameter spotsize was used in limited tests of 6 to 8 J/cm<sup>2</sup>, but excessive dermal damage was noted. This is consistent with findings presented in Tan et al., "Spotsize effects on guinea pig skin following pulsed irradiation," The Journal of Investigative Dermatology, Vol. 90, No. 6, June 1988. At all pulse durations, incomplete lightening was found at 2 J/cm<sup>2</sup> and 2.5 J/cm<sup>2</sup>. The 3.0 J/cm<sup>2</sup> was found to be the most effective dose. The 3.5 J/cm<sup>2</sup> was only used in a limited number of tests where insufficient response was obtained at 3.0 J/cm<sup>2</sup> and was effective. With the 1  $\mu$ sec pulse duration, the lesions cleared but recurred. At 500 nsec, nonrecurring clearance was obtained. At 250 nsec, clearance was also obtained, and we are awaiting final results. Clinical observations indicate minimal dermal damage without noticeable pigmentary incontinence.

30 With limited tests at 504 nm and 4 J/cm<sup>2</sup>, some permanent loss of normal pigment and undesirable surface changes were noted. However, with appropriate selection of other parameters, higher fluences may be feasible.

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Limited tests of a 694 nm Q-switched ruby laser having a pulse duration of 20 nsec and fluence of  $5 \text{ J/cm}^2$  proved ineffective in removing the superficial lesions. Similarly, a Q-switched alexandrite laser of 760 nm, 100 nsec and  $3 \text{ J/cm}^2$  was ineffective in treating the superficial lesion with a 2mm spotsize.

Limited tests at 577 nm, 360 nsec resulted in clearance of the lesion but with recurrence. However, lesions are expected to be effectively treated with that wavelength at shorter pulse durations. To minimize adverse effects, particularly due to pigmentary incontinence, wavelengths of about 600 nm or less are judged best from the first set of experiments.

Although 504 nm is the shortest wavelength tested, it is the most effective, and it is expected that shorter wavelengths within the melanin absorption spectrum will provide desirable results. Due to concerns for mutagenesis, wavelengths of less than 345 nm should not be used. It is postulated that the shorter wavelengths are most effective with least damage because they are absorbed by blood in the dermis and thus create thermal effects which minimize pigmentary incontinence.

It is expected that the acceptable fluence range at the skin is a function of wavelengths. At 504 nm, some effect on melanin is noted at  $2 \text{ J/cm}^2$ , and damage is seen above  $4 \text{ J/cm}^2$ . The depth of penetration in caucasian skin, which is inversely related to absorption, for 350 nm, 500 nm, 600 nm and 700 nm is about  $60 \mu$ ,  $230 \mu$ ,  $550 \mu$  and  $750 \mu$ , respectively. Thus, expected ranges of effect without damage, based on the 2 to  $4 \text{ J/cm}^2$  range at 504 nm, is about 0.5 to  $1.0 \text{ J/cm}^2$  for 345 nm, and 5 to  $10 \text{ J/cm}^2$  for 600 nm. In general, it is expected that fluences of 1 to  $10 \text{ J/cm}^2$  at the skin will be used for

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wavelengths of 345 nm to 600 nm. Thus, the first laser configured to provide a beam having these parameters may be employed to effectively treat epidermal pigmentation abnormalities.

5 On the other hand, treatment of pigmentation abnormalities in the dermis are also of interest, and longer wavelengths have been shown to be more effective due to greater depths of penetration. Tattoo treatment with a Q-switched ruby laser was studied by clinical  
10 assessment as presented in Taylor et al., "Treatment of Tattoos by Q-Switched Ruby Laser," Arch. Dermatology, Vol 126, July 1990. The tattoos were exposed to 694 nm laser irradiation. Pulse durations of 40 to 80 nsec with fluence ranging from 1.5 to 8 J/cm<sup>2</sup> for each pulse  
15 duration. All tattoos contained blue-black pigment and a few also had small areas of red, yellow, or green. It was demonstrated that the blue-black tattoos responded well to ruby laser treatment. However, the green and yellow areas responded less than well and the red areas  
20 responded poorly or not at all.

A problem encountered with laser treatment using longer wavelength beams is that of pigmentary incontinence where pigment from the epidermis is driven to the lower dermis. One means of treating the deeper  
25 lesions with longer wavelengths without pigmentary incontinence is to remove the pigment in the epidermis using the shorter wavelengths and subsequently treat the lower regions with longer wavelengths before normal epidermal pigment returns. Thus, the shorter wavelengths  
30 remove the pigment from the epidermis to create a window through which the light can pass into the dermis. Without pigment in the epidermis, illumination using the

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longer wavelengths cannot cause the pigmentary incontinence.

Effective treatment with minimal damage should be achieved with the second laser having a wavelength of about 750 nm, a pulse duration of about 100 nsec and a fluence of about  $1 \text{ J/cm}^2$  at the skin. The second beam may provide a fluence ranging from 1 to  $10 \text{ J/cm}^2$  at the skin through a range of wavelengths between 600 and 1100 nm. The longer wavelengths are optimal to achieve the depths of penetration associated with deeper pigmentation abnormalities including pigmented lesions and tattoos.

Based on the aforementioned tests, the present invention comprises a pair of lasers each providing a pulsed beam of laser radiation having specific parameters for obtaining effective treatment of epidermal and dermal pigmentation abnormalities while minimizing damage to normal pigmented cells. Effective treatment of epidermal pigmentation abnormalities may be achieved by employing a first beam having a wavelength between 345 and 600 nm, a pulse duration of less than  $1 \mu\text{sec}$ , and a fluence between 1 and  $10 \text{ J/cm}^2$  at the skin. Additionally, effective treatment of dermal pigmentation abnormalities may be achieved by employing a second beam having a wavelength between 600 and 1100 nm, a pulse duration of less than 500 nsec and a fluence between 1 and  $10 \text{ J/cm}^2$  at the skin. In a typical dermatology procedure, such treatment is administered by delivering laser radiation from the lasers to the skin with a delivery system.

Because the present invention requires pulse durations on the order of tens of nanoseconds to hundreds of nanoseconds and potentially high power densities, the delivery system must be capable of transmitting high peak intensity pulses with minimal losses and must be flexible

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for convenience of use. An articulated arm multiple mirror system has been used for high peak power applications in a dermatology procedure and may be employed. However, an articulated arm is bulky, cumbersome and difficult to align. Multifiber bundle cables are not appropriate because of high transmission losses related to the core/clad ratio. A flexible solid core single optical fiber is generally one of the most convenient delivery means for delivering a beam of laser radiation to illuminate a pigmented region of skin. A solid core fiber smaller than about 1 mm in diameter would be required because a larger fiber is too rigid. However, the maximum power density a 1 mm solid fiber can transmit is about  $5 \text{ MW/mm}^2$ . Since peak laser beam intensities in the present invention may be up to ten times the maximum power density of the fiber (i.e. up to about  $46 \text{ MW/mm}^2$ ), the fiber will be damaged or destroyed. A large diameter fiber would be required to handle the peak intensities, but such a fiber would be inflexible. Thus, solid core single optical fibers are not suitable delivery systems for the dual laser system.

The present invention employs a delivery system capable of transmitting high peak intensity pulses of wavelength between 345 and 1100 nm with minimal loss and which is flexible for convenience of use. In one preferred embodiment, shown in Fig. 1, the delivery system 13 comprises a pair of liquid core light guides 14 and 15 for delivery of laser radiation in dermatology procedures. The light guides are flexible and have a sufficient core diameter to transmit high peak intensity pulses of laser radiation with low losses. More specifically, the first liquid core light guide 14 delivers the first beam of laser radiation of wavelength

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between 345 and 600 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 1  $\mu$ sec to the handpiece 16 for treatment of epidermal pigmentation abnormalities. The second liquid core light guide 15 delivers the second beam of laser radiation of wavelength between 600 and 1100 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 500 nsec to the handpiece 17 for treatment of dermal pigmentation abnormalities such as deeper pigmented lesions and tattoos.

A cross-sectional view of a liquid core light guide 40 is presented in Fig. 6. In one embodiment, the guide has a liquid core 42 comprising a liquid 43 which allows the transmission of light having a wavelength between 345 and 600 nm through the guide. The liquid core is housed in a flexible, thermostable, plastic cladding 44. The cladding has a lower refractive index than the liquid, producing total internal reflection at the core/clad interface such that light may be transmitted around bends in the light guide. Thus, the flexible guide transmits light independent of its configuration. The guide has an core diameter in the range of 3 to 10 mm and preferably about 3 mm such that the guide is capable of transmitting high peak power density pulses of laser radiation. These laser pulses enter and exit the guide 40 at a pair of silica rod windows 45 which also seal liquid with the guide. A metallic monocoil tube 46 surrounding the cladding has tooth-like contour which facilitates flexibility. A pair of end pieces 50 fasten around the windows and secure the cladding and the monocoil tube. An outer sleeve 48 encloses the monocoil tube and provides outer mechanical protection.

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Experiments have shown that a flexible liquid core light guide, made by Lumatec GmbH, having an aqueous inorganic salt solution within the liquid core, performs well in the spectral region from about 400 to 600 nm.

5 More specifically, the light guide 14 (made by Lumatec) has been used with a laser which produces 2 J, 300 nsec, 1 to 10 J/cm<sup>2</sup> pulses at a wavelength of 510 nm to effectively treat epidermal pigmented lesions.

Although the first liquid core light guide 14 has  
10 been shown to effectively deliver pulsed laser radiation in the spectral range from about 400 to 600 nm, it does not effectively transmit laser radiation of wavelengths between 600 and 1100 nm (red and near infrared wavelengths). The poor transmission capability of the  
15 liquid of the first guide in the red and near infrared spectral range is due to the presence of chemical bonds involving hydrogen in the molecular structure of the liquid in the core. Overtone and combination bands of fundamental frequencies associated with such bonds lead  
20 to absorption coefficients which are large enough to significantly attenuate the beam of pulsed laser radiation over distances required for convenient delivery (approximately 1.5 meters). Thus, to effectively transmit laser radiation from the second laser, the  
25 second liquid core light guide must employ a liquid having no chemical bonds involving hydrogen or any other bonds which lead to absorption in the range of 600 to 1100 nm. Further, it has been determined that the liquid must satisfy other criteria relating to its physical  
30 properties including low volatility, low gain coefficients for stimulated scattering and acceptable index of refraction as explained below.

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Two classes of chemical compounds having no chemical bonds that lead to the aforementioned absorption are completely deuterated compounds and halogenated compounds, specifically halocarbons. Within these two classes, the selected compound must be a liquid so that the guide remains flexible. Additionally, the compound must have low gain coefficients which provide an indication of the likelihood of stimulated scattering processes (Brillouin and Raman scattering) for a given laser peak power density. The gain coefficients must be sufficiently low such that the peak power density to be transmitted is below the critical intensity for the threshold of these non-linear scattering effects. Furthermore, the refractive index of the liquid must be greater than the refractive index of the cladding for the guide to transmit radiation with minimal losses. If an otherwise suitable liquid comprising a deuterated compound such as deuterium oxide has an unacceptably low index of refraction, a solute such as an inorganic salt may be added to increase its index to an acceptable value.

A light guide comprising the halocarbon carbon tetrachloride has been tested as the core liquid. In accordance with the above-described parameters, the light guide cladding material had an index of refraction of about 1.4 and the core liquid had an index of refraction of about 1.5. Alexandrite laser pulses at a wavelength of 760 nm, energy of 1 J and 55 ns pulse duration were successfully transmitted at 80% over 1.5 meters in guide having a 5 mm diameter core. The output spectrum from the guide was observed and showed no evidence of wavelength shifts produced by stimulated scattering. Additionally, the halocarbon tetrachloroethylene has been



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tested with alexandrite laser pulses up to 600 mJ and demonstrates the same percentage transmission.

In another preferred embodiment, shown in Fig. 5, the delivery system 13 comprises a single liquid core light guide 15 for efficiently transmitting high peak power intensity pulses of wavelengths between 345 and 1100 nm from the dual laser system. The light guide 15 comprises a liquid 43 capable of transmitting laser radiation in the wavelength range of the first laser as well as the second laser. As such, the light guide 15 is coupled to both lasers via an optical coupler 38 and delivers radiation provided by the first laser for treatment of epidermal pigmentation abnormalities and radiation provided by the second laser for treatment of dermal pigmentation abnormalities.

While this invention has been particularly shown and described with references to preferred embodiments thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention as defined by the appended claims. For example, other classes of chemical compounds having no chemical bonds which lead to absorption within the 600 to 1100 nm range may be used. Thus, the liquid within the second light guide may comprise silicate compounds or nitrile compounds.

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CLAIMS

1. An apparatus for treating epidermal and dermal pigmentation abnormalities of the skin comprising:
  - 5 a first pulsed laser for treating epidermal pigmentation abnormalities by providing a first beam of wavelength between 345 and 600 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 1  $\mu$ sec;
  - 10 a second pulsed laser for treating dermal pigmentation abnormalities by providing a second beam of wavelength between 600 and 1100 nm, fluence of 1 to 10 J/cm<sup>2</sup> at the skin and pulse duration of less than 0.5 nsec; and
  - 15 a delivery system coupled to the first and second lasers for delivery of the first and second laser beams to illuminate the epidermal and dermal pigmented lesions respectively.
- 20 2. An apparatus as claimed in Claim 1 wherein the first laser is a dye laser and the second laser is an alexandrite laser.
3. An apparatus as claimed in Claims 1 wherein the first and second lasers are dye lasers.
- 25 4. An apparatus as claimed in Claim 1, 2 or 3 wherein the first laser produces a beam of about 500 nm wavelength, 3 J/cm<sup>2</sup> fluence at the skin, and 500 nsec or less pulse duration.

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5. An apparatus as claimed in Claim 1, 2, 3 or 4 wherein the delivery system illuminates a region of about 2 to 5 mm diameter.
- 5 6. An apparatus as claimed in Claim 1, 2, 3, or 4 wherein delivery system illuminates a region of about 3 mm diameter.
7. An apparatus as claimed in Claim 1, 2, 3, 4, 5, 6 or 7 wherein the delivery system comprises a flexible liquid core light guide for delivery of the first and second laser beams.
- 10 8. An apparatus as claimed in Claim 1, 2, 3, 4, 5, or 6 wherein the delivery system comprises a flexible liquid core light guide for delivery of the second laser beam.
- 15 9. An apparatus as claimed in Claim 7 or 8 wherein the liquid core light guide comprises a liquid having a molecular structure characterized by the absence of chemical bonds that cause the absorption of light having wavelengths between 600 and 1100 nm.
- 20 10. An apparatus as claimed in Claim 7 or 8 wherein the liquid core light comprises a non-hydrogenous liquid.
11. An apparatus as claimed in Claim 9 or 10 wherein the liquid comprises halogenated compounds.
- 25 12. An apparatus as claimed in Claim 9 or 10 wherein the liquid has a molecular structure which comprises halocarbons.

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13. An apparatus as claimed in Claim 9 or 10 wherein the liquid comprises tetrachloroethylene.
14. An apparatus as claimed in Claim 9 or wherein the liquid comprises deuterium oxide and inorganic salts.
15. An apparatus as claimed in Claim 9 or 10 wherein the liquid comprises carbon tetrachloride.
16. An apparatus as claimed in Claim 9 or 10 wherein the guide has a core diameter of about 5 mm.
- 10 17. An apparatus as claimed in Claim 9, 10, 11, 12, 13, 14, 15 or 16 wherein the liquid core light guide further comprises a flexible, thermostable cladding in which the liquid is located, wherein the liquid has a refractive index which is greater than the cladding refractive index.
- 15 18. An apparatus as claimed in Claim 1, 2, 3, 4, 5, 6 or 7 wherein the delivery system comprises a liquid core light for delivery of the first laser beam and an articulated arm for delivery of the second laser beam.
- 20 19. An apparatus as claimed in Claim 8 wherein the delivery system comprises a second flexible liquid core light for delivery of the first laser beam.

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20. A dermatology laser apparatus comprising:  
a pulsed laser for dermatology procedures on a  
subject's skin by providing a beam of wavelength  
between 345 and 1100 nm, fluence of 1 to 10 J/cm<sup>2</sup> at  
the skin and pulse duration of less than 1 μsec; and  
a flexible liquid core light guide for delivery  
of the beam to illuminate an area on the subject's  
skin.
21. An apparatus as claimed in Claim 20 wherein the  
light guide has a core diameter between 3 and 10 mm.
22. An apparatus as claimed in Claim 20 or 21 wherein  
the light guide has a core diameter of about 5 mm.
23. An apparatus as claimed in Claim 19, 20, 21 or 22  
wherein the light guide further comprises a  
flexible, thermostable cladding in which a liquid is  
located, the liquid having a greater refractive  
index than the cladding.
24. An apparatus as claimed in Claim 23 wherein the  
light guide further comprises a pair of windows  
located at each end of the guide and which seal a  
liquid within the cladding and a flexible metallic  
monocoil tube enclosing the cladding.
25. An apparatus as claimed in Claim 19, 20, 21, 22, 23  
or 24 wherein the liquid core light guide comprises  
a non-hydrogenous liquid.

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26. An apparatus as claimed in Claim 19, 20, 21, 22, 23 or 24 wherein the liquid core light guide comprises a liquid having a molecular structure characterized by the absence of chemical bonds that cause the absorption of light having wavelengths between 600 and 1100 nm.
27. An apparatus as claimed in Claim 19, 20, 21, 22, 23, 24, 25 or 26 wherein the liquid has a molecular structure which comprises halocarbons.
28. An apparatus as claimed in Claim 19, 20, 21, 22, 23, 24, 25, 26 or 27 wherein the liquid comprises tetrachloroethylene.
29. An apparatus as claimed in Claim 19, 20, 21, 22, 23, 24, 25, 26 or 27 wherein the liquid comprises carbon tetrachloride.
30. An apparatus as claimed in Claim 19, 20, 21, 22, 23, 24, 25 or 26 wherein the liquid comprises deuterated compounds and inorganic salts.
31. A liquid core light guide having a core diameter of about 5 mm and capable of transmitting a beam of laser radiation of a wavelength between 600 and 1100 nm and a fluence of at least  $1 \text{ J/cm}^2$ , said light guide comprising a liquid having a molecular structure characterized by the absence of chemical bonds that cause the absorption of light having wavelengths between 600 and 1100 nm.

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32. An apparatus as claimed in Claim 31 wherein the core diameter is between 3 and 10 mm.
33. An apparatus as claimed in Claim 30, 31 or 32 wherein the light guide further comprises a flexible, thermostable cladding in which the liquid is located, the cladding having a refractive index which is less than the refractive index of the liquid.
34. An apparatus as claimed in Claim 30, 31, 32 or 33 wherein the light guide further comprises a pair of windows located at each end of the guide and which seal the liquid within the cladding and a flexible metallic monocoil tube enclosing the cladding.
35. An apparatus as claimed in Claim 30, 31, 32, 33 or 34 wherein the liquid comprises halogenated compounds.
36. An apparatus as claimed in Claim 30, 31, 32, 33, 34 or 35 wherein the liquid has a molecular structure which comprises halocarbons.
37. An apparatus as claimed in Claim 30, 31, 32, 33, 34, 35 or 36 wherein the liquid comprises tetrachloroethylene.
38. An apparatus as claimed in Claim 30, 31, 32, 33, 34, 35 or 36 wherein the liquid comprises carbon tetrachloride.

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39. An apparatus as claimed in Claim 30, 31, 32, 33 or 34 wherein the liquid comprises deuterated compounds and inorganic salts.



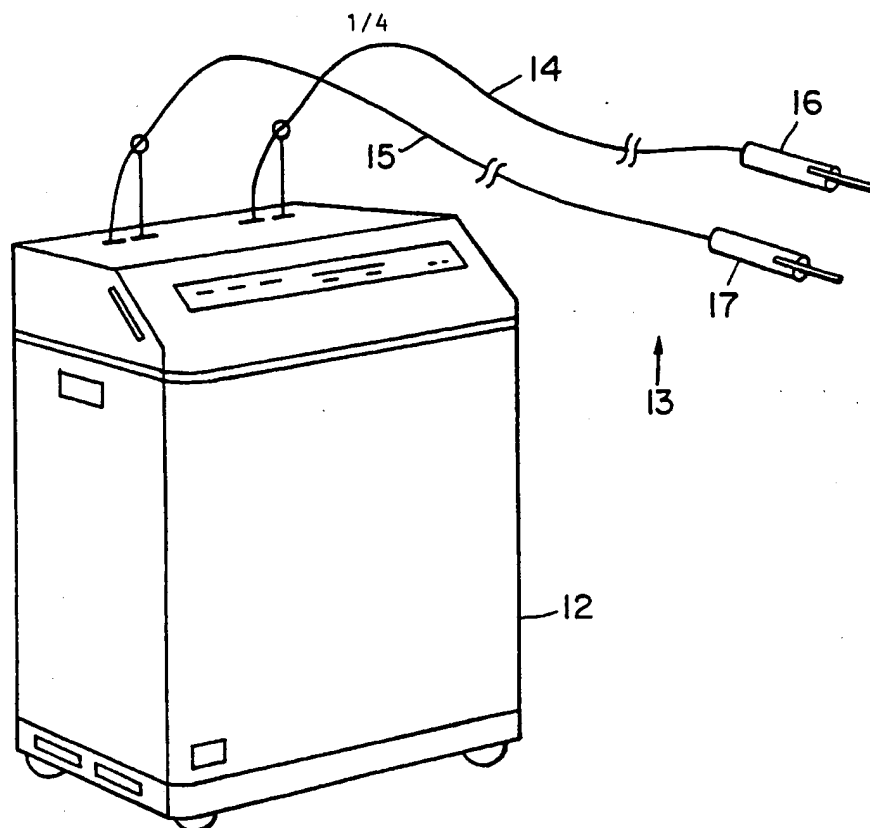


Fig. 1

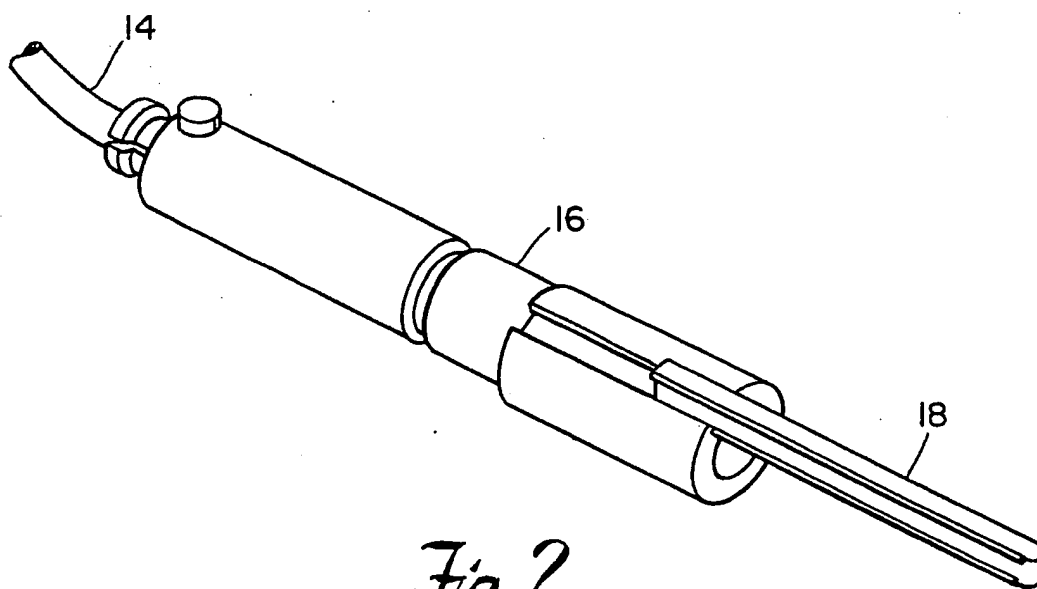
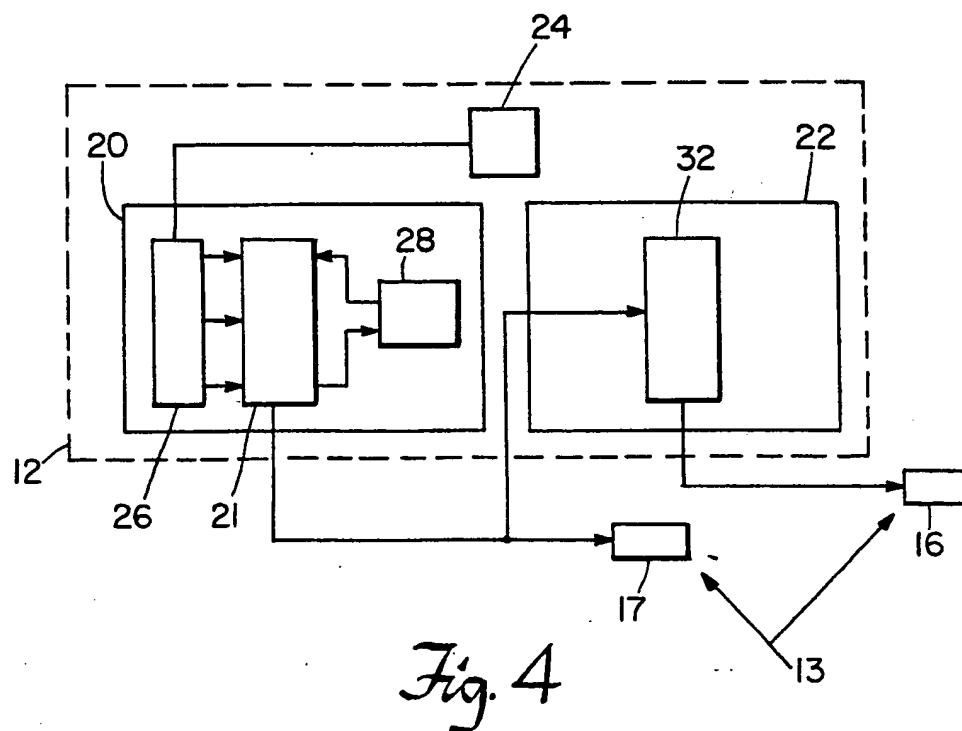
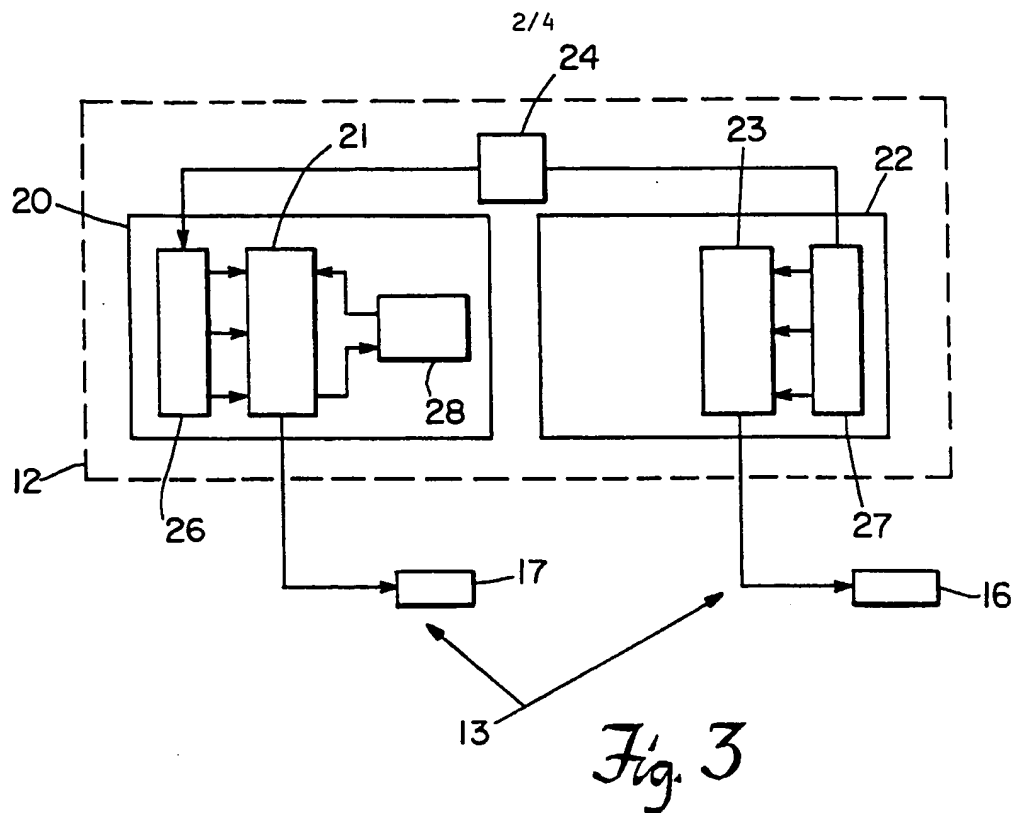
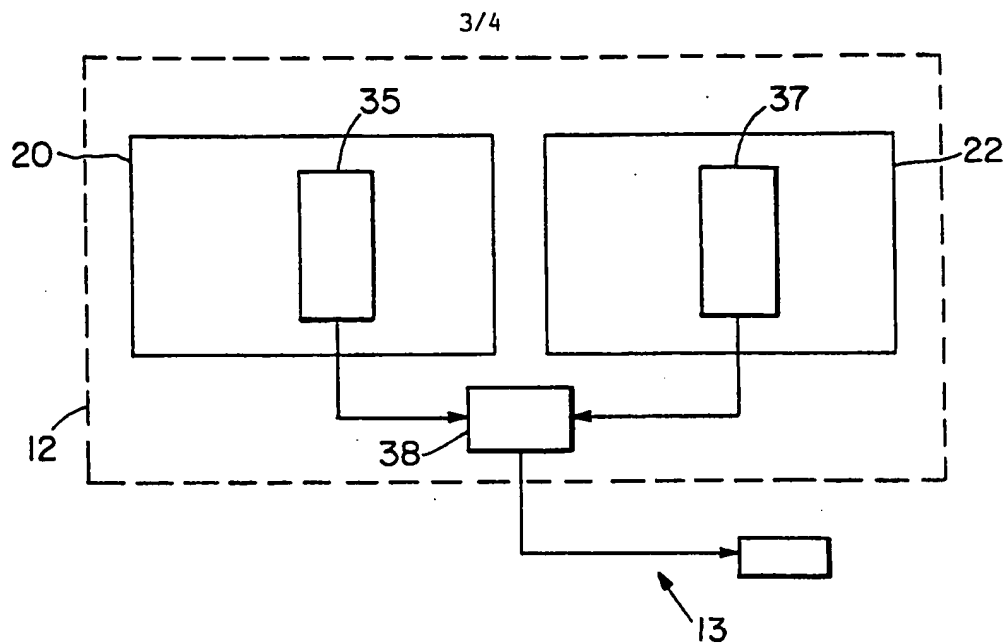


Fig. 2



*Fig. 5*

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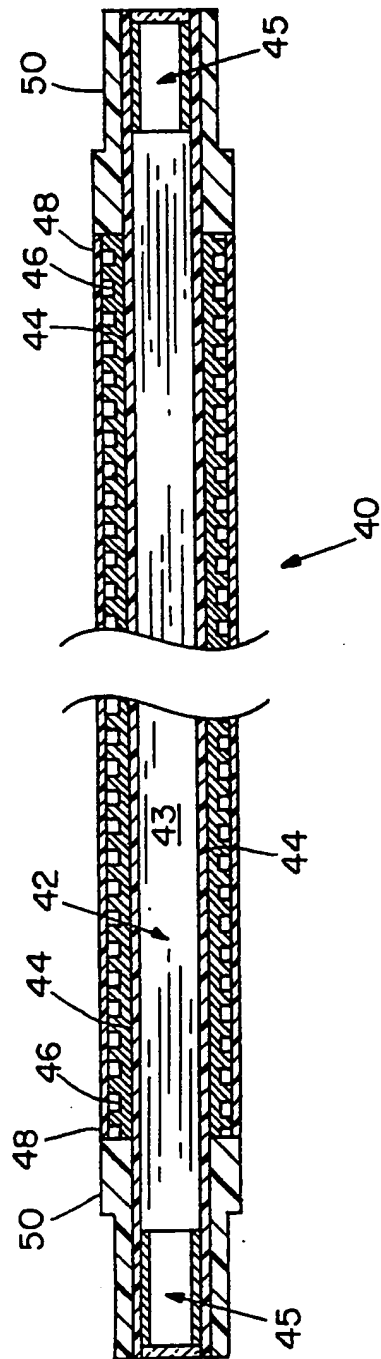



Fig. 6

## INTERNATIONAL SEARCH REPORT

PCT/US 91/01714

International Application No

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (If several classification symbols apply, indicate all) <sup>6</sup>		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. 5      A61N5/06		
<b>II. FIELDS SEARCHED</b>		
Minimum Documentation Searched <sup>7</sup>		
Classification System	Classification Symbols	
Int.Cl. 5	A61N ;      G02B	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>		
<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT<sup>9</sup></b>		
Category <sup>10</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
A	DE,A,2308554 (NATH) 22 August 1974 see the whole document	1-12, 15-19, 23-27, 29 30-36, 38
A	WO,A,8704632 (MÜLLER) 13 August 1987 see pages 4 - 6	1-6
Y	Lasers in Surgery and Medicine vol. 1, 1981, USA pages 263 - 276; R.Anderson & J.Parrish: "Microvasculature can be selectively damaged using dye lasers: a basic theorie and experimental evidence in human skin"	20-39
Y	EP,A,246552 (HOECHST AG) 25 November 1987 see page 4, lines 28 - 49	20-39
<p><sup>10</sup> Special categories of cited documents : <sup>10</sup></p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&amp;" document member of the same patent family</p>		
<b>IV. CERTIFICATION</b>		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
09 JULY 1991	18. 07. 91	
International Searching Authority	Signature of Authorized Officer	
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**ANNEX TO THE INTERNATIONAL SEARCH REPORT  
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**US 9101714**

**SA 46082**

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**09/07/91**

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		EP-A- 0257052	02-03-88
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EP-A-246552	25-11-87	DE-A- 3617005	26-11-87
		JP-A- 62287207	14-12-87
		US-A- 4747662	31-05-88

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